REMARKS

Reconsideration and withdrawal of the rejections of record are respectfully requested in view of the amendments and remarks contained herein.

Claims 1, 5-9, and 51 remain pending in this application.

Requirement for New Title

As required by the Examiner, Applicants have amended the title to be more clearly indicative of the invention to which the claims are directed.

Rejection of Claims 1, 5-9 and 51 Under 35 U.S.C. § 112, First Paragraph

Scope of Enablement

The Examiner states that "[c]laims 1, 5-9, and 51 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for identifying certain organisms, does not reasonably provide enablement for identification of any type of pathogen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims."

The applicant respectfully traverses this rejection. It is respectfully pointed out to the Examiner that the fact that some experimentation maybe necessary does not preclude enablement. Rather, the amount of experimentation simply must not be undue. The present invention employs a varied range of phlyogenetically diverse pathogens such as bacteria, viruses, fungi, and components thereof to demonstrate that the exposure of dendritic cells to a pathogen results in a pathogen-specific pattern of gene expression. The methodology employed by the invention, namely contacting the pathogen (or its immunogenic components) to the dendritic cells, isolating and labeling of mRNA from the dendritic cells, detecting of mRNA from the dendritic cells to generate a gene profile, and subsequently analyzing this gene profile remains the same across a varied range of phylogenetically diverse pathogens including bacteria, viruses, fungi, and components thereof. In Example 1 of the invention, the identical methodology is employed against pathogens as diverse as polyI:C, *E. Coli*, Influenza, LPS, *C. Albicans*, mannan, and combinations thereof. See Specification, page 23. In Example 2, oligonucleotide

microarrays were used to test to what extent dendritic cells discriminate between phylogenetically diverse pathogens which included a gram-negative bacterial species, *E. Coli* and its cell wall component, LPS, a fungus, *C. Albicans*, and yeast cell wall-derived mannan, and RNA virus, influenza A, and double-stranded RNA (dsRNA). The amount of experimentation required to adapt the practice of determining a gene expression response of dendritic cells from that seen for pathogens as diverse as bacteria, viruses, and fungi to other pathogens in the environment is not unduly burdensome.

Furthermore, the state of the art, combined with the teachings of the invention provide one of ordinary skill in the art a complete understanding of the biological responses elicited by dendritic cells exposed to pathogens. Dendritic cells are known to those of ordinary skill in the art as being professional antigen presenting cells residing in most tissues where they survey for incoming pathogens. It is also known to those skilled in the art that the capacity of dendritic cells to recognize invading pathogens and become activated is the first critical event in the initiation of the immune response. The invention teaches that dendritic cells can discriminate between phylogenetically varied pathogens (See Examples 1 and 2 of the disclosure).

Thus, one of ordinary skill in the art would reasonably believe that the disclosure is supportive of the full scope of the claims.

Reconsideration and withdrawal of the rejection are respectfully requested.

Lack of Enablement

The Examiner states that "[c]laims l, 5-9, and 51 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention." Specifically, the Examiner states that "[c]laims 1, 5, 9, and 51 are directed to identifying a pathogen by noting stimulus specific genes that are specific to a particular pathogen . . . " and that ". . . this very broad assertion cannot stand based solely on the three types of pathogens used."

The applicant respectfully traverses this rejection. It is respectfully pointed out to the Examiner that claims 1, 5-9, and 51 are directed to a method to identify a pathogen by

determining genes that are specific to a particular pathogen. As shown in Examples 1 and 2 of the disclosure, some of these genes are common to diverse pathogens, while others are specific to certain classes of pathogens, or specific pathogens. The invention also teaches that the presence of pathogen-specific gene expression in most functional categories (including transcription factors and cytokines) suggests that distinct pathways are activated by different pathogens, even as common responses to varied classes of pathogens may also exist (See Example 2, page 32 of the disclosure). The specificity or commonality of the genes regulated by the exposure of the cells to the pathogen may be determined by one skilled in the art using biological techniques disclosed in the specification or otherwise commonly known to those skilled in the art.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claim 8 Under 35 U.S.C. § 112, Second Paragraph

The Examiner states that "[c]laim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Claim 8 recites the word "common" which is vague and indefinite. It is unclear what the metes and bounds are for this term. Clarification of this issue via clearer claim wording is requested."

The applicant respectfully traverses this rejection. It is respectfully pointed out to the Examiner that the specification provides a definition of the term "common." The patentee, as his own lexicographer, has clearly set forth a definition of the disputed claim term on page 13 of the specification. The invention teaches that "'[c]ommon stimulus-responsive genes,' as used herein, refer to genes that are regulated in response to two or more pathogens, pathogen classes, or components thereof. 'Common stimulus-responsive' and 'common regulated' genes can be used interchangeably."

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1, 5-9 and 51 Under 35 U.S.C. § 103(a)

Claims 1, 5-9, and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cummings *et al.* (Genomics, Vol. 6, No. 5, Sept-Oct 2000, pages 513-525) in view of Hashimoto *et al.* (Blood, Vol. 96, No. 6, September 2000) and Cirillo (WO 02/08418).

It is respectfully pointed out to the Examiner that a proper rejection based on 35 U.S.C. § 103 that relies on a combination of prior art references, requires a teaching, suggestion, or motivation to combine the teachings of the references a reasonable expectation of success founded in the cited art of producing the claimed invention; and that such proper combination teaches or suggests all elements of the claimed invention. The applicant respectfully traverses this rejection for failing to meet all of these requirements for the reasons provided below.

It is respectfully pointed out to the Examiner that Cummings teaches the use of DNA micoarrays to study host-DNA interactions using cell systems. However, Cummings does not teach host-DNA interactions in dendritic cells. Moreover, Cummings does not teach a standard methodology by which to identify pathogens as claimed in the present invention, nor does Cummings specifically describe the use of dendritic cells or immature dendritic cells. Hashimoto teaches the use of SAGE to identify expressed genes when dendritic cells are stimulated by LPS, a factor normally involved in the maturation process. When LPS stimulates dendritic cells, the expressed genes vary from those expressed by immature unstimulated dendritic cells. Thus, Hashimoto teaches that microbial and inflammatory factors cause differential gene expression between mature and immature dendritic cells to vary, thus providing information on the process of cell differentiation. Hashimoto, however, does not teach that dendritic cells may be used successfully to distinguish between pathogens. Nowhere does Hashimoto teach that dendritic cells may be used to differentiate or distinguish between different pathogens. Furthermore, while Hashimoto teaches that dendritic cell maturation is influenced by a variety of factors, Hashimoto also teaches that all these factors lead to a single result, *i.e.*, dendritic cell maturation. See Hashimoto, page 2206, Col. 1. Thus, Hashimoto not only fails to teach that dendritic cells may be used to differentiate between pathogens based on differential gene expressions caused in dendritic cells, it teaches away from the teaching of the present

invention by suggesting that a variety of microbial and inflammatory factors lead to one end result, that of cell maturation. It is also pointed out to the Examiner that Cirillo teaches the use of a primary cell type infected by the known pathogen of interest, *i.e.* monocytes. Cirillo does not teach a standardized method in which cell response may be used as a sensor to distinguish between different pathogens.

It is respectfully pointed out to the Examiner that the use of dendritic cells is an essential element of the present invention, allowing for successful differentiation between pathogens. Cummings does not teach the use of dendritic cells. Although, Hashimoto teaches the use of dendritic cells, Hashimoto does not teach that dendritic cells can distinguish and/or differentiate between pathogens. In fact, Hashimoto teaches away from the invention by suggesting that a variety of microbial and inflammatory factors lead to one end result, that of cell maturation. Cirillo fails to teach a method by which dendritic cells can be used to distinguish between different pathogens. The present invention, however, teaches that dendritic cells can be used to identify pathogens based on analyzing the gene profile generated by contacting the pathogen with the dendritic cell. Thus, Hashimoto not only fails to provide a suggestion or motivation to combine its teachings with that of Cummings, it also fails to provide any reasonable expectation of success if such teachings are combined. Furthermore, the combined teachings of Cummings, Hashimoto and Cirillo do not provide a motivation to combine the aforementioned references to teach the elements of the invention, namely the use of dendritic cells to distinguish between pathogens. Moreover, this latter combination of references fails to provide a reasonable expectation of success because it teaches away from the desired result. Thus, one of skill in the art would not have been motivated to use the teachings of Cummings, with Hashimoto and Cirillo to use dendritic cells as sensors to distinguish between pathogens.

Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the amendments and remarks above, Applicants believe all pending claims are in condition for allowance.

If the Examiner believes that a conference would be of value in expediting the prosecution of this application, the Examiner is hereby invited to telephone undersigned counsel to arrange for such a conference.

Respectfully submitted,

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